

Appl. No. 09/926,491
Amendment dated: October 14, 2003
Reply to OA of: April 7, 2003

Amendments to the Specification:

On page 57, please replace Example 13 in its entirety which ends on page 59 with the following amended Example 13. (The underlining has been deleted throughout the Example in order for the corrections to be underlined and for the convenience of the Examiner.)

Example 13

a) **3-Triisopropylsilyloxy-20-epi-23,23a-bishomo-19-nor-chol-1,3,5(10),16-tetraene-24-nitrile [Formula (II): $R^3 = \beta\text{-CH}_3$, $R^4 = (i\text{-Pr})_3\text{Si}$, $R^5 = \text{H}$, $Y = (\text{CH}_2)_4$, $\Delta 16$ double bond]**

C1
Treatment of the bromide from Preparation 8(g) (350 mg) with the lithium salt of acetonitrile according to the procedure of Example 3(a) gave the title compound: IR ν_{max} 2250, 1610, 1450-1600 (3 bands) cm^{-1} ; NMR (CDCl_3) δ 0.78 (s, 18-H's), 5.2 (bs, 16-H), 6.5, 6.95 (m, 1-, 2- and 4-H's).

b) **25-Amino-3-triisopropylsilyloxy-20-epi-24-homo-19-nor-cholest-1,3,5(10),16-tetraene [Formula (I): $R^1 = R^2 = \text{CH}_3$, $R^3 = \beta\text{-CH}_3$, $R^4 = (i\text{-Pr})_3\text{Si-}$, $R^5 = \text{H}$, $X = \text{NH}_2$, $Y = -(\text{CH}_2)_4$, $\Delta 16$ double bond]**

The nitrile from (a) above was treated with cerium chloride/methyl lithium according to the procedure of Example 3(b) to give the title compound (100mg): IR (CDCl_3) ν_{max} 1610, 1450-1600 (3 bands) cm^{-1} ; NMR (CDCl_3) δ 0.78 (s, 18-H's), 1.2 (26,27-H's), 5.2 (bs, 16-H), 6.5, 6.95 (m, 1-, 2- and 4-H's).

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c) **25-Amino-3-hydroxy-20-epi-24-homo-19-nor-cholest-1,3,5(10),16-tetraene**
[Formula (I): $R^1 = R^2 = CH_3$, $R^3 = \beta-CH_3$, $R^4 = R^5 = H$, $X = NH_2$, $Y = (CH_2)_4$, $\Delta 16$ double bond]

The silyl ether from (b) above (40 mg) was desilylated as in Example 1(d) to give the title compound: IR (CDCl₃) ν_{max} 3600, 1615, 1450-1600 (2 bands) cm⁻¹; NMR (CDCl₃) δ 0.78 (s, 18-H's), 1.05 (d, 21-H's), 1.2 (26,27-H's), 3.9 (bs, 3H [exchanges with D₂O] - OH, NH's), 5.2 (bs, 16-H), 6.5, 6.95 (m, 1-, 2- and 4-H's).

d) **25-Acetylimino-3-triisopropylsilyloxy-20-epi-24-homo-19-nor-cholest-1,3,5(10),16-tetraene** [Formula (I): $R^1 = R^2 = CH_3$, $R^3 = \beta-CH_3$, $R^4 = (i-Pr)_3Si$, $R^5 = H$, $X = NH(COCH_3)$, $Y = (CH_2)_4$, $\Delta 16$ double bond]

The silyl ether from (b) above (60 mg) was acetylated as in Example 3(c) to give the title compound: IR (CDCl₃) ν_{max} 3420, 1660, 1610, 1450-1600 (2 bands) cm⁻¹; NMR (CDCl₃) δ 0.78 (s, 18-H's), 1.2 (26,27-H's), 1.9 (bs, NH), 5.2 (bs, 16-H), 6.5, 6.95 (m, 1-, 2- and 4-H's).

e) **25-Acetylamino-3-hydroxy-20-epi-24-homo-19-nor-cholest-1,3,5(10),16-tetraene** [Formula (I): $R^1 = R^2 = CH_3$, $R^3 = \beta-CH_3$, $R^4 = R^5 = H$, $X = NH(COCH_3)$, $Y = -(CH_2)_4$, $\Delta 16$ double bond]

The silyl ether from (d) above (60 mg) was desilylated as in Example 1(d) to give the title compound (36 mg): IR ν_{max} 3420, 1610, 1665, 1450-1600 (2 bands) cm⁻¹; NMR (CDCl₃) δ 0.78 (s, 18-H's), 1.2 (26,27-H's), 1.9 (bs, NH), 5.2 (bs, 16-H), 6.5, 6.95 (m, 1-, 2- and 4-H's).

f) **25-Amino-3-hydroxy-20-epi-19-nor-cholest-1,3,5(10),16-tetraene** [Formula (I): $R^1 = R^2 = CH_3$, $R^3 = \beta-CH_3$, $R^4 = R^5 = H$, $X = NH_2$, $Y = (CH_2)_3$, $\Delta 16$ double bond]

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This is prepared by substituting sodium cyanide for the anion in step (a) above and thereafter following the procedures of steps (b) and (c) above.

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cont.
g) **25-Acetylamino-3-hydroxy-20-epi-24-homo-19-nor-cholest-1,3,5(10),16-tetraene** [Formula (I): $R^1 = R^2 = CH_3$, $R^3 = \beta-CH_3$, $R^4 = R^5 = H$, $X = [(NH_2)] NH(COCH_3)$, $Y = (CH_2)_3$, $\Delta 16$ double bond]

This is prepared by substituting sodium cyanide for the anion in step (a) above and thereafter following the procedures of steps [(a),] (b), (d) and [(d)] (e) above.
